

Appl. No. 10/526,822  
Reply to Office Action of May 22, 2007

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### REMARKS/ARGUMENTS

In the amendments, the surfactant of means 1) recited in amended claims 1 and 5 is limited to "polyoxyethylene hydrogenated castor oil 60 or polyoxyl 35 castor oil", and means 3) recited in amended claims 1 and 5 is amended to recite "adding a tonicity agent consisting essentially of a nonionic tonicity agent." Further, claims 3 and 7 are canceled due to the incorporation of part of these claims into claims 1 and 5.

#### Support of Amendments

Please note that amendments with respect to means 1) of claims 1 and 5 are supported by the description of the present specification, page 6, lines 3 to 4, Example 1-2, Example 1-3, Formulation 2, and Formulation 3, where ophthalmic solutions containing either "polyoxyethylene hydrogenated castor oil 60" or "polyoxyl 35 castor oil" as a surfactant are described.

With respect to means 3) of claims 1 and 5, the amendments made this time are supported by the description of the present specification, page 4, lines 2-7 from the bottom, and, page 7, lines 4-8, which describe that the use of the salts as a tonicity agent is a cause of the white

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turbidity and that white turbidity can be prevented by using a nonionic tonicity agent as a tonicity agent.

Moreover, it is noted that Formulations 6 to 10 are actually clear ophthalmic solutions (see Table 8), that none of these Formulations comprise salts (ionic tonicity agents) such as sodium chloride as the tonicity agents, and that these Formulations all comprise tonicity agents consisting of non ionic tonicity agents.

It is therefore submitted that the amendments do not incorporate new matter.

Claims 1-10 are rejected under 35 USC 103(a) as being unpatentable over Dean et al (U.S. Patent 6,166,073), the Patent Abstract of Japan and further over Hellberg et al (U.S. Patent 6,646,001).

None of the references describe the ophthalmic solution of the present invention as now claimed. Thus, the present Invention is novel.

The rejection as set forth above, is one of obviousness over the art combination.

According to the present specification, the inventors first confirmed the problem of white turbidity due to a change of formulation in ophthalmic solutions containing latanoprost at a certain concentration and benzalkonium chloride at a certain

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concentration. To avoid the problems, they found three means 1) to 3) (see Claim 1) for preventing the white turbidity, and thereby solved the problem (See the present specification page 3, line 13 to page 4, line 7).

Concerning the issue of considering the art to solve the problem, it is noted that none of the references describe or suggest at all the above-mentioned problem. In view thereof, it is not surprising that the art does not show or suggest means for solving the problem. Therefore, it is impossible even for the skilled in the art to lead to the present invention from the cited references, which do not describe the problem or a means for solving the problem.

None of the References Describe the Problem or its  
Solution

Dean et al. (U.S. Patent 6,166,073) merely describe compositions containing DP-agonist and FP-agonist prostaglandin agonists for treating glaucoma or ocular hypertension. Dean et al do not describe or suggest at all the problem of white turbidity due to a change of formulation in ophthalmic solutions containing latanoprost and benzalkonium chloride. Further, Dean et al do not describe or suggest any means for preventing white turbidity in claim 1.

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The Patent Abstract of Japan merely describes a method of producing aqueous tonicity solution, comprising using polyhydric alcohol as a tonicity agent. There is no description or suggestion at all in the Patent Abstract of Japan not only about the change of formulation but also about latanoprost.

Hellberg et al (U.S. Patent 6,646,001) merely describe compositions for the treatment of glaucoma and ocular hypertension, comprising a prostaglandin FP receptor agonist and a prostaglandin synthesis inhibitor. Hellberg et al do not describe or suggest at all the problem of white turbidity due to a change of formulation in ophthalmic solutions containing latanoprost and benzalkonium chloride. Further, Hallberg et al do not describe or suggest at all the means for preventing white turbidity. Although Hallberg et al describe in Example 4 compositions comprising latanoprost, benzalkonium chloride, and Polysorbate 80, it is not known from the description of Hallberg et al. whether the formulation of Example 4 is a clear solution or an opaque one.

As discussed above, none of the references describe or suggest at all the problem that white turbidity is observed due to a change of formulation in ophthalmic solutions containing latanoprost at a certain concentration and benzalkonium chloride at a certain concentration.

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To solve the problem, the present invention uses one of the means 1) to 3) in order to prevent white turbidity due to a change of formulation.

First of all, in means 1), polyoxyethylene hydrogenated castor oil 60" or "polyoxyl 35 castor oil" is contained as a surfactant in order to overcome the problem of white turbidity. There is no reason to lead to an ophthalmic composition containing such a surfactant, based on the combined teaching of the reference where the problem of white turbidity is not described.

Furthermore, the present invention according to means 1) exhibits a novel effect of preventing white turbidity, which is not a problem to be solved in the references but in the present invention, and therefore, such an effect can not be obvious from the references where even the problem of white turbidity is not described. Hence, an ophthalmic solution formulated according to means 1) of the present invention exhibits a novel effect and an unexpected effect.

Second, in means 2), benzalkonium chloride having 12 carbon atoms is used. Since none of the references describe the problem of white turbidity or even a

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benzalkonium chloride having 12 carbon atoms, they cannot be combined in any way to lead to an ophthalmic solution wherein benzalkonium chloride having 12 carbon atoms is used as a means for solving the problem. Moreover, as with the present invention according to means 1), the present invention according to means 2) also exhibits a novel effect of preventing white turbidity, which is not a problem to be solved in the references but in the present invention, and therefore, such an effect can not be obvious from the references where even the problem of white turbidity is not described. Hence, an ophthalmic solution formulated according to means 2) of the present invention exhibits a novel and unexpected effect.

Finally, in means 3), a tonicity agent consisting essentially of a nonionic tonicity agent is added whereby white turbidity due to a change of formulation is prevented. This means is introduced following the inventor's focus on the fact that the use of the salts as a tonicity agent is a cause of white turbidity. Accordingly, an ophthalmic solution wherein a nonionic tonicity agent alone is essentially added as a tonicity agent, as a means for solving the problem, is not obvious or shown in the art. Moreover, as with the present invention according to means 1), the present invention according to means 3) also exhibits a

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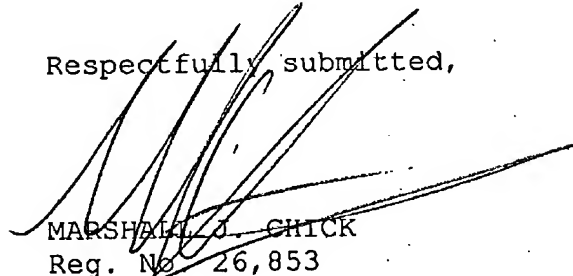
novel effect of preventing white turbidity, which is not a problem to be solved in the references but in the present invention, and therefore, such an effect can not be obvious from the references where even the problem of white turbidity is not described. Therefore, an ophthalmic solution formulated according to means 3) of the present invention exhibits a novel effect, or an unexpected effect.

As discussed above, the present invention can not be obtained from the references taken alone or in combination. Absent from the art is a description or suggestion of the problem to be solved by the present invention or the solution to the problem. No combination of art provides the means or teaching.

In view of the above, the rejections are avoided. Allowance of the application is therefore respectfully requested.

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Respectfully submitted,



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